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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,647	01/07/2002	Toni Marie Antalis	11168A	3669

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EXAMINER	
MONSHIPOURI, MARYAM	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 03/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,647	ANTALIS ET AL.	
	Examiner	Art Unit	
	Maryam Monshipouri	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 66-76 is/are pending in the application.

4a) Of the above claim(s) 67,69,70 and 73 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 66,68,71,72 and 74-76 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/023942.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's response to restriction letter filed 1/3/2005 is acknowledged. Applicant elected Group II invention directed to claims 66, 68, 71-72 and 74-76, drawn to SEQ ID NO:5 with traverse. Claims 67, 69-70, and 73, SEQ ID NO:3, 28, 29-30 are withdrawn as drawn to non-elected invention.

In traversal of restriction requirement applicant argues the following: **(1)** that isoforms "L" and "S" of HELA2 testisin proteinase, and proteinases encoded by SP001LA, SP002LA and SP003LA genes are related and are not independent and distinct and should be kept together.

(2) restriction letter indicated that Groups I- V belong to the same class and subclass and MPEP section 808.02 states that "where however, the classification is the same and the field of search is the same and there is no clear indication of separate future field of search, no reasons exist for dividing among related inventions". Thus, in accordance with MPEP, there is no reason for dividing the single invention of the present application into Groups I-V. Applicant then provides additional arguments against relying on classification as a basis for requiring restriction.

(3) In view of continued increase of official fees and the potential limitation of an applicant's financial resources, a practice by the Office which arbitrarily imposes restriction requirements should be avoided. Further, it is vital to all applicants that restriction requirements issue with the proper statutory authorization because patents issuing on divisional applications which are filed to prosecute claims that the examiner held to be independent and distinct can be vulnerable to legal challenges alleging double patenting.

(4) that in view of the arguments provided above imposition of restriction requirement with inadequate authority can lead to situations in which an applicant's legitimate patent rights are exposed to uncertainly and even extinguished and determination to make the pending restriction requirement final must evidence the patentable distinctness evidence of all defined five groups and hence, reconsideration and withdrawal of restriction is requested.

These arguments are fully considered but were found **unpersuasive** for the following reasons: with respect to applicant's **first** argument applicant fails to indicate in which way said proteins are related. Applicant is requested to review the contents of the specification (page 51, and Figure 17) wherein both isoforms of HELA2(testisin) are disclosed. According to said disclosure the two isoforms of said HELA2 proteins are generated through the use of two alternative mRNA splice sites and preliminary molecular modeling shows that the presence of 6 nucleotides insertion in the gene encoding the " L" isoform is likely to alter the catalytic activity and/or specificity of HELA2(testisin) for its substrates. Hence, as applicant can appreciate, the two isoforms of HELA2 have different nucleotide composition and their expression products have different catalytic activities and substrate specificities, and are clearly patentably distinct.

With respect to expression products of SP001-3LA genes being related to HELA2 isoforms the examiner once again would like to draw the attention of the applicant to Example13 and pages 51-52 of the specification wherein it has been shown that SPL001-3LA only display 35-40% similarity to cDNA encoding HELA2 protein and said

similarity is barely sufficient to claim that all SPL001-3LA genes or expression products thereof are related to HELA2 proteins or their encoding genes. Further, in view of the examiner absent direct evidence, in contrast to applicant's position, proximity of a gene to that with a known function on a chromosome, does not automatically imply that the proximal gene has the same function and as the gene with known function. Applicant is further reminded that he/she has not even displayed assay results for the expression products of SPL001-3LA genes in order to convince the skilled artisan that said gene products are in fact proteinases and in view of said ambiguities PL001-3LA gene products are most probably not proteinases and should not even have been placed in the same class/subclass as proteinases in the previous office action.

In response to applicant's **second** argument, firstly the examiner would like to indicate that she did not justify restricting the inventions based on their separate class/subclasses. As applicant is aware the criteria for restriction in the previous office action was based on recognized divergent subject matter and not class/subclass. Thus, applicant's arguments with regards to classification not being a reliable base for holding restriction is irrelevant. Secondly, as explained in detail above, based on evidence of record it is not even clear that SPL0001-3 LA genes encode proteinases. Therefore it is totally puzzling hew applicant indicates that said proteins are related and should be considered as a single invention.

With respect to applicant's **third** argument even though examiner is in full sympathy with the applicant that increase in filing fees may impose a limitation on applicant's financial resources she merely restricts the inventions based on 35 U.S.C.

section 121 and not on the financial resources of the applicant and restriction under said section is totally proper. Applicant may not need to worry about the vulnerability of his/her patent to double patenting challenges because clearly this is not the case here.

Finally, in view of applicants **fourth** argument, based on the response and evidence provided above, as well reasons provided in the previous office action, the examiner feels that the restriction imposition is done with more than adequate authority and said restriction fails to expose applicant's legitimate patent rights to uncertainty.

Restriction is hereby made final.

DETAILED ACTION

Claims 66, 68, 71-72 and 74-76, SEQ ID NO:5 only, are under examination on the merits.

Claim Objections

Claims 66, 68, 72 are objected to because of the following informalities: said claims still recite non-elected subject matter. Applicant is advised to rewrite said claims such that they only recite SEQ ID NO:5, which is the elected subject matter. Appropriate correction is required.

Information Disclosure Statement

It is noted that applicant has submitted a 1449 form with the IDS paper filed 1/7/2002. However said form is currently missing in the scanned application. Applicant is advised to resubmit said form and relevant references in response to this office action

so that the examiner would be able to examine its contents before drafting her next office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first and second paragraphs of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
>
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 66, 68, 72, 74-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "medium stringency" in claims 66, 68, 72, and 74 is unclear. Applicant has not defined this term in the specification. In the absence of a clear salt conditions associated with said term one of skill in the art does not know how to prepare the products claimed. Claims 75-76 are merely rejected for depending from rejected base claims.

Claim 66, 68, 72, 74-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase " hybridizing to any of those sequences " in claims 66, 72, and 75-76 is unclear. It is not clear which DNA sequences applicant is referring to SEQ ID NO:5, 50% homologs of SEQ ID NO:5, or complements of 50% homologs of SEQ ID NO:5. Appropriate clarification is required.

Claim 72, 74-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. The term "derivative" in claims 72, and 74 and their dependent claims 75-76 is unclear. Applicant has not defined said term in the specification. Appropriate clarification is required.

Claims 66, 68, 71-72, 74-76 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for expression product of SEQ ID NO:5, does not reasonably provide enablement for isolated serine proteinases encoded by nucleotide sequences having at least 50% similarity to SEQ ID NO:5 or complement thereof, or proteinases encoded by a nucleotide sequence capable of hybridizing to SEQ ID NO:5 or complements thereof under medium stringency conditions at 42 °C as well as proteinases having at least 50% similarity to SEQ ID NO:6.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2n 1400 (Fed. Cir. 1988) are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. The specification fails to teach which critical nucleotides in: 50% homologs of SEQ ID NO:5, complements thereof, nucleotides that hybridize to SEQ ID NO:5 or hybridize to 50% homologs of SEQ ID NO:5, under medium stringency conditions, should be retained such that the expression products of said sequences would retain serine proteinase activity. The disclosure likewise fails to teach which amino acids in SEQ ID NO:6 should be retained such that 50% homologs of SEQ ID NO:6 would be able to retain proteniase activity. No examples of such residues are provided either. Current

state of prior art indicates that once 5-6 nucleotides of a sequence encoding a full-length polypeptide are mutated said mutant is not necessarily going to encode a product with the activity corresponding to said full-length polypeptide . Similarly, according to prior art once 3-4 amino acids of a full-length proteinase is mutated said mutant is not necessarily going to retain proteinase activity.

Therefore due to lack of sufficient teachings and examples provided in the specification and due to unpredictability of prior art as to which residues within claimed polynucleotides, homologs or complements thereof are in charge of assigning function to their expression products the skilled artisan has to go through the burden of undue experimentation in order to screen for those DNA sequences that are within the scope of this invention (i.e. encode serine proteinase) and as such the claims go beyond the scope of the disclosure.

Similarly due to lack of sufficient teachings and examples provided in the specification and due to unpredictability of prior art as to which residues within claimed proteinase are in charge of retaining function the skilled artisan has to go through the burden of undue experimentation in order to screen for those polypeptides that are within the scope of this invention (i.e. have serine proteinase activity) and as such the claims go beyond the scope of the disclosure.

Since the polypeptides of claims 66, 68, 71, 72 and 74 are not enabled, compositions comprising said products (claims 75-76) are not enabled either.

Claims 66, 68, 71-72 and 74-76 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s)

contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 66, 68, 71, 72 and 74 are directed to the following **genera** of polypeptides which have been inadequately described in the specification:

1) a **genus** of proteinases encoded by 50% homologs of SEQ ID NO:5 or complements thereof.

2) a **genus** of proteinases having at least 50% similarity to SEQ ID NO:6.

3) a **genus** of proteinases encoded by nucleotide sequences that hybridize to SEQ ID NO:5 under "medium" stringency conditions.

4) a **genus** of proteinases encoded by DNA sequences that hybridize to 50% homologs of SEQ ID NO:5, under "medium" stringency conditions.

The specification does not contain any disclosure of the structure of all DNA sequences that are encoding the polypeptides listed as 1-4 above. The genus of polypeptides that comprise these above products is a large variable genus with the potentiality of retaining many different structures. Therefore, many structurally unrelated products are encompassed within the scope of these claims. Considering the scope of these claims, which allows for 157 (i.e. 50%) of total amino acids of SEQ ID NO:6 to be mutated and considering the fact that once more than 3-4 amino acids of a full-length polypeptide is mutated, it is likely that said mutant will no longer be able to retain its three dimensional structure to retain proteinase activity some description of

where within said proteinase homologs must the mutations occur is necessary, which is currently lacking in the specification.

The specification discloses only **a single species (SEQ ID NO:6)** for each claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Since the products of claims 66 and 74 are lacking written description the compositions comprising said products (claims 75-76) also lack written description.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

No claims are allowed.

Allowable Subject Matter

SEQ ID NO:6 is allowed. This is because said amino acid sequences is free of prior art. Further the prior art does not teach pr suggest preparing such specifically claimed amino acid sequence. Hence said sequence is also non-obvious.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maryam Monshipouri whose telephone number is (571) 272-0932. The examiner can normally be reached on 7:00 a.m to 4:30 p.m. except for alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnanthapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MCMonshi

Maryam Monshipouri Ph.D.

Primary Examiner

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